IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Tagg *et al.*
Serial No.	:	09/913,763
Filed	:	August 17, 2001
For	:	LANTIBIOTIC
Art Unit	:	1651
Examiner	:	Michael V. Meller

745 Fifth Avenue, New York, NY 10151

EXPEDITED PROCEDURE
RESPONSE AFTER FINAL ACTION
UNDER 37 C.F.R. 1.116

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: **Mail Stop AF Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**, on October 3, 2003.

Marilyn Matthes Brogan, Reg. No. 31,223

Name of Applicant, Assignee or Registered Representative

Signature

October 3, 2003

Date of Signature

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, John Robert Tagg, do hereby declare and state that:

1. I am an Australian citizen and live in Dunedin, New Zealand.

2. I am a Professor of Microbiology at the University of Otago, Leith Street, Dunedin, New Zealand. I am a scientific consultant to Blis Technologies Limited and my brief curriculum vitae is attached as Exhibit 1.

3. I am an inventor of the above-identified patent application.

4. I have read the Office Action on this application dated 3 June 2003.

5. The Salivaricin B protein from *Streptococcus mitus*, described in the Declaration that was executed by me on March 12, 2003 and filed on March 18, 2003, was isolated and identified according to teachings provided in the present application.

and identify the protein of claim 4 without undue experimentation. Well-known techniques in molecular biology can be employed to either manipulate the protein of SEQ ID NO:3 by inserting, deleting or substituting from one to three amino acid residues, or to identify a protein that differs from that of SEQ ID NO:3 by the insertion, deletion or substitution of from one to three amino acid residues. Established microbiological techniques, as were used in the experiments described in the specification, can be used to determine whether the protein is bacteriocidal. Therefore, the skilled artisan would be able to envision and arrive at the full scope of the claimed invention, using the instant application and his or her own knowledge at the time of filing.

7. Further, *Streptococcus salivarius* strains K12 and K30 were isolated for the first time by me from saliva samples obtained from human subjects by plating out on *Mitis Salivarius* agar, and have been held in my personal collection since.

8. Neither the strains, *per se*, nor details of same have been made publicly available prior to filing this patent application or its priority forming application filed 12 October 1999.

9. These strains were found to be unusual in that they inhibited the growth of all 9 indicator bacteria in our standardised BLIS production typing technique. Previously we had found that *S. salivarius* strains producing the lantibiotic *salivaricin A* gave inhibition of 8 of these 9 indicators.

10. It was found, by me, that strains K12 and K30 produced two lantibiotics not previously detected - *salivaricin A_2* (a variant of *salivaricin A*) and *salivaricin B*.

11. Only approximately 5% of *S. salivarius* strains subsequently tested produce inhibition of all 9 indicators and can be shown to have the structural genes for and ability to express *salivaricin B*.

12. As far as I am aware, no strains of *S. salivarius* producing *salivaricin A_2* and *salivaricin B* have been identified and characterised prior to my isolating and characterising strains K12 and K30.

13. It is also noteworthy that *salivaricin A_2* seems to be the form of *salivaricin A* that is produced by strains of *S. salivarius* that also produce *salivaricin B*.

14. I declare that all statements herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful and false statements and

the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

John Robert Tagg

20/9/03

Date

Attachment: Curriculum Vitae

EXHIBIT 1

CURRICULUM VITAE

Full name: Dr John R. Tagg

Present position: Professor in Microbiology

Present employer: University of Otago

Present work address: Department of Microbiology
University of Otago
PO Box 56 Dunedin

Academic qualifications:

BSc	Melbourne University	Microbiology 1967
MSc	Melbourne University	Microbiology 1969
PhD	Monash University	Microbiology 1972

Years as a practising researcher: 29

Honours/distinctions/membership of societies, institutions, committees:
Commonwealth Postgraduate Award (1967) American Heart Association Fellowship (1972) Member American Society for Microbiology and NZ Microbiological Society. Committee member, Treasurer, Vice-president and President of NZMS during the period 1990 -1997. Convernor Otago University Hands-on Science Summer School and Executive Member of Dunedin International Science Festival.

Previous positions held:
Post-doctoral Associate of the American Heart Association in the Pediatrics Department, University of Minnesota1972-1974
Lecturer, Department of Microbiology, Otago University 1975-1979
Senior Lecturer, Microbiology Department , Otago University 1979-1991
Associate Professor, Department of Microbiology, Otago University 1992-2001

Present research/professional speciality:
Streptococcal infections and their control using bacteriocin-like inhibitory substances (BLIS)

International Collaborations:
USA: Microbiology and Immunology Department, University of Oklahoma, Joint Project, Genetic studies of lantibiotic production, 1992.
Germany: Department of Medical Microbiology, University of Bonn, Purification and mode of action studies of staphylococcal BLIS, 1990 -present.
Denmark: Department of Medical Microbiology, University of Aarhus, BLIS production by oral streptococci, 1995 - present.
England: University of Bristol, Marsden Grant collaboration with Prof. Howard

EXHIBIT 1

Jenkinson, 1996 – 2000.

Number of refereed publications: 115

1. Major publications (in the last five years)

Wescombe, P. A. and Tagg J.R. Purification and characterisation of streptin, a type A1 lantibiotic produced by Streptococcus pyogenes In Press Appl. Environ. Microbiol Tagg J.R.and Dierksen K.P. Bacterial replacement therapy: adapting germ warfare to infection prevention. In Press. Trends in Biotech Balakrishnan, M., Simmonds R. S., Kilian M. and Tagg J. R. Different bacteriocin activities of Streptococcus mutans reflect distinct phylogenetic lineages. J. Med Microbiol. 51:941-948 (2002) Upton, M., Tagg, J.R., Wescombe, P. and Jenkinson, H.F. Intra- and interspecies signaling between Streptococcus salivarius and Streptococcus pyogenes mediated by SalA and SalA1 lantibiotic peptides. J. Bacteriol.
183: 3931-3938 (2001)
Martin D.R. and J. R. Tagg. Streptococci and Streptococcal Diseases Entering the New Millennium. Wellington, Securacopy (2000) 926p Balakrishnan, M., Simmonds, R.S and Tagg, J.R. Dental caries is a preventable infectious disease. Aust. Dent. J. 45: 235-245 (2000) Dierksen, K.P., Ragland, N.L. and Tagg, J.R. A new alkaline pH-adjusted medium enhances detection of ß-hemolytic streptococci by minimizing bacterial interference due to Streptococcus salivarius. J. Clin. Microbiol.
38: 643-650 (2000)
Balakrishnan, M., Simmonds, R.S. Carne, A. and Tagg, J.R. Streptococcus mutans strain N produces a novel low molecular mass non-lantibiotic bacteriocin. FEMS Microbiol. Lett. 183: 165-169 (2000) Dierksen, K.P. and Tagg, J.R. Haemolysin-deficient variants of Streptococcus pyogenes and S. dysgalactiae subsp equisimilis may be overlooked as aetiological agents of pharyngitis? J. Med. Microbiol. 49: 811-816 (2000) Dierksen, K.P., Inglis, M. and Tagg, J.R. High pharyngeal carriage raters of Streptococcus pyogenes in Dunedin schoolchildren with a low incidence of rheumatic fever. NZ Med. J. 113: 496-499 (2000) Balakrishnan M., Simmonds R. S. and Tagg J. R. Diverse activity spectra of bacteriocin-like inhibitory substances (BLIS) having activity against mutans streptococci. Caries Res. 35: 75-80 (2000) Navaratna, M. A. D. B., Sahl, H-G. and Tagg J.R. Identification of genes encoding two-component lantibiotic production in Staphylococcus aureus strain C55 and other phage group II S. aureus strains and demonstration of an association with the exfoliative toxin B gene. Infect. Immun. 67:
4268-4271(1999)
Navaratna, M. A. D. B., Sahl, H-G. and Tagg J.R. Two-component anti-Staphylococcus aureus lantibiotic activity produced by Staphylococcus aureus strain C55. Appl. Environ. Microbiol. 64: 4803-4808 (1998) Tompkins, G.R., Peavey, M.A., Birchmeier, K.R. and Tagg, J.R. Relationships of bacteriocin production and sensitivity to interbacterial coaggregation and genetic competence of oral streptococci. Oral Microbiol. Immunol. 12: 98-105 (1997) Simmonds, R.S., Simpson, W.J. and Tagg J.R.. Cloning and sequence analysis of zooA, a Streptococcus zooepidemicus gene encoding a bacteriocin-like inhibitory substance having a domain structure similar to that of lysostaphin. Gene 189: 255-261 (1997)

EXHIBIT 1

2. Major achievements in commercial, social and environmental areas.
Scientific consultant to BLIS Technologies Ltd). The first product (BLIS K12 Throat Guard) was developed on the basis of research done in my laboratory. Further products based on other strains developed in my laboratory and intended to prevent a variety of bacterial infections of humans and other animals are under development.

3. Demonstration of relationships with end-users.
Frequent communicator to the general public via the press, radio and television. A "60 Minutes" item featuring the research in my laboratory appeared last year on TV1. Items on BLIS this year are incorporated within the Natural History New Zealand production "Microbe Invasion" and the Beyond Productions film "Hot Science in New Zealand" scheduled for showing on the Discovery and National Geographic channels respectively. Regularly invited to chair sessions at national and international conferences in the fields of streptococcal and bacteriocin research. Vice Chairman of the Organising Committee for the XIV Lancefield International Symposium on Streptococci and Streptococcal Diseases held in Auckland, October 11-15, 1999.

Consultant and contract researcher to Unilever Research, Port Sunlight, England (1991-1994) to evaluate the potential commercial application of streptococcal bacteriocins to the prevention of dental caries.

Consultant and contract researcher to Lactose New Zealand (1998-2000) to investigate the production of the lantibiotic nisin.

Consultant and contract researcher to Kiwi Dairies Co. (1999) to develop novel products containing streptococcal BLIS

Consultant and contract researcher to the New Zealand Dairy Board (1997-2000) to study:
(i) the potential for incorporation of nisin into cheese products;
(ii) milk peptides with anti-bacterial activity; and
(iii) the potential applications of BLIS-producing streptococci